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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,031	03/30/2001	Muthiah Manoharan	ISIS-4723	1044

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

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DATE MAILED: 07/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant(s)

09/823,031

Applicant(s)

MANOHARAN ET AL.

Examiner

Janet L. Epps-Ford, Ph.D.

Art Unit

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-60 is/are pending in the application.
- 4a) Of the above claim(s) 1-21 and 40-49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-39 and 50-60 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments

2. Claims 22-39 and 50-60 remain rejected under 35 U.S.C. 103(a) as being anticipated by Guzaev et al. (US 5,959,090), for the reasons of record set forth in the Official Action mailed 2-11-03.

3. Applicant's arguments filed 4-29-03 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the Guzaev patent does not disclose a method for preparing oligonucleotides to which a conjugate group is attached. Applicants argue that one of ordinary skill in the art would not consider a phosphate group to be a conjugate group. According to Applicant, the specification as filed lists a variety of conjugate groups, namely intercalators, reporter molecules, polyamines, polyamides, polyethylene glycols, and polyethers as exemplary conjugate groups that can be attached to oligonucleotides using the claimed methods, see page 11, lines 26 to page 13 line 26 of the specification as filed. Moreover, in regards to the intermediates described in col. 4 of Guzaev, Applicants argue that those of ordinary skill in the art would understand that conjugate groups are to remain attached to an oligonucleotide and are not protecting groups that are removed during synthesis or preparation of the oligonucleotide.

Applicant's arguments are not persuasive because col. 4, lines 8-44, clearly show the conjugation of a phosphate containing building block that comprises a 4,4-dimethoxytrityl group, and two electron-withdrawing groups (such as amide and esters; R1 and R2). Moreover, the

Art Unit: 1635

building block addition to oligonucleotides allows the ordinary artisan to determine coupling efficiency by conventional dimethoxytrityl assay, however, prior approaches to oligonucleotide synthesis suffered from the shortcoming of not allowing final coupling efficiency. Moreover, although Applicants consider the derivatized oligonucleotides of col. 4 to be intermediates, nonetheless the formation of this intermediate confers properties to the modified oligonucleotide that are advantageous to oligonucleotide synthesis in comparison to unmodified oligonucleotides. Therefore, the modified intermediate oligonucleotide has utility. Contrary to Applicant's assertions, the oligonucleotides of Guzaev having a phosphoramidite building block according to formula (1) at either the 5' or 3' end comprise a conjugation group according to the present invention. Additionally, in regards to the addition of a 5' or 3' phosphate group to an oligonucleotide, this modification allows oligonucleotides comprising this modification to be used for gene construction, cloning, mutagenesis, and the ligation chain reaction, whereas unmodified oligonucleotide require treatment with a kinase prior to their use in these processes. Therefore, in comparison to unmodified oligonucleotides, the phosphorylated oligonucleotides of Guzaev are encompassed by the instantly claimed invention, which recite oligonucleotides comprising a conjugate group. Moreover, it is noted that limitations corresponding to the exemplary conjugate groups described in the specification as filed are not included in the instant claims. Moreover, it is noted that Applicant's own definition of the term "conjugate group" is not limited to the specific groups listed in the specification as filed, since the specification as filed (page 11, lines 28-32) clearly states "[C]onjugate groups of the invention *include* intercalators, reporter molecules, ..." This definition clearly suggests that the conjugate groups contemplated by the specification as filed are not limited to the exemplary groups set forth in the

Art Unit: 1635

specification as filed. Office personnel are to give claims their broadest reasonable interpretation in light of the supporting disclosure. Limitations appearing in the specification, but not recited in the claim are not read into the claims. (See MPEP § 2106.)

As stated in the prior Office Action, the invention as a whole would have been *prima facie* over Guzaev et al. at the time of filing of the instant application.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Art Unit: 1635

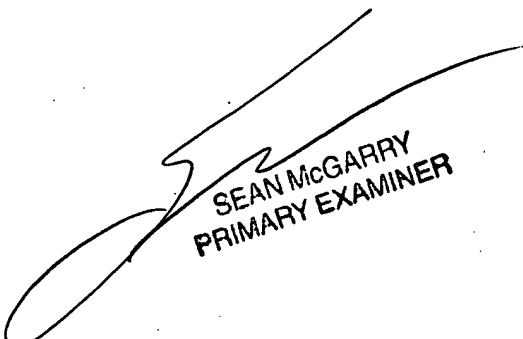
5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Fri, 8:30AM-6:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L. Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
July 13, 2003



SEAN MCGARRY
PRIMARY EXAMINER